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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,564	02/18/2004	James P. Quigley	1361.036US1	9290
21186 7590 05/18/2007 SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A. P.O. BOX 2938 MINNEAPOLIS, MN 55402			EXAMINER SANG, HONG	
			ART UNIT 1643	PAPER NUMBER
			MAIL DATE 05/18/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/781,564

Applicant(s)

QUIGLEY ET AL.

Examiner

Hong Sang

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 34-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Exhibit A</u> . |

DETAILED ACTION

RE: Quigley et al

1. Applicant's response filed on 4/4/2007 is acknowledged. Claims 1 and 34-36 are pending. New claims 34-36 are added. Claims 2-33 are cancelled.
2. Claims 1 and 34-36 are under examination.

Rejections Withdrawn

3. The rejection of claim 32 under 35 U.S.C. 112, first paragraph because of new matter is withdrawn in view of applicants' cancellation of the claim.

Response to Arguments

4. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Scherl-Mostageer et al. (Oncogene, 2001, 20: 4402-4408, IDS) is maintained.

The response states that the corrected sequence is not necessarily "inherent" in the CDCP1 protein discussed in the Scherl-Mostageer's reference. The response states that the original sequence shown in Figure 2 of the Scherl-Mostagger et al reference, which differs from SEQ ID NO.1 at positions 525 and 827, indicates that Scherl-Mostagger et al. did not, in fact, have a protein sequence of SEQ ID NO.1. The response states that Scherl-Mostageer et al. obtained the CDCP1 sequence from sequencing a PCR product amplified from a cDNA library, which itself was generated by reverse transcription from isolated RNA, since "errors" could be introduced during reverse transcription to generate the cDNA product or during amplification to generate

the PCR product, the "correct" sequence is not necessarily an inherent feature in the Scherl-Mostagger et al.'s original CDCP 1 sequence.

Applicants' arguments have been carefully considered but are not found persuasive. While the sequence shown in Figure 2 of Scherl-Mostageer's reference is not identical to the instant SEQ ID NO.1, this sequence was corrected and the corrected sequence is 100% identical to the instant SEQ ID NO.1 (see the Exhibit C enclosed in the previous office action, page 1, lines 6-7, and the sequence alignment pages 4-5). Because it is the same protein or DNA encoding the protein that was sequenced again, the later published sequence (corrected sequence) is an inherent property of that protein. Applicants made assertion that an error could have been introduced during reverse transcription. However applicants did not present any evidence to support their assertion. Applicants did not present evidence that the two sequences were not derived from the same protein. Furthermore, the search databases (STN database) clearly show that the protein sequence is updated for the very same protein (also see Exhibit C enclosed in the previous office action, page 1, lines 6-7), as such the rejection is deemed proper and therefore maintained.

New Grounds of Rejections

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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6. Claims 34-36 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 34-36, as written, do not sufficiently distinguish over proteins (variants) as they exist naturally because claims do not particularly point out any non-naturally occurring differences between the claimed proteins (variants) and the naturally occurring protein (variants).

In the absence of the hand of man, the naturally occurring proteins and peptides are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" variant or similar language would obviate this rejection.

Claim Rejections - 35 USC § 112, 1st paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 34-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Applicants broadly claim a variant of SEQ ID NO, wherein the variant has glutamine as amino acid 525, aspartic acid as amino acid 709 or asparagines as amino acid 827.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

Because claim recites the term "has", which is open language, claims do not limit the variants to have just a single amino acid change at the specified position (i.e. 525, 709, or 827) within the full length of SEQ ID NO.1. Claims encompass a genus of proteins or fragments, which have glutamine as amino acid 525, aspartic acid as amino

acid 709 or asparagines as amino acid 827. Such proteins or peptides can have multiple amino acid changes at any positions of SEQ ID NO.1, or fragments thereof. Therefore, claims encompass undefined and uncharacterized protein variants.

Quantity of experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the structure and function of the claimed variants.

Moreover, the claims are broadly drawn to any variants with or without the biological properties of SEQ ID NO.1. The specification does not teach how to make and use the claimed variants.

The state of the prior art and the predictability or lack thereof in the art:

Protein chemistry is probably one of the most unpredictable areas of biotechnology. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, conservative replacement of a single "lysine" residue at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial

loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2).

Working examples:

The specification teaches identification of the protein of SEQ ID NO.1, and cloning of the mRNA encoding the variant of SEQ ID NO.1, wherein the amino acid 525 is glutamine, the amino acid 709 is aspartic acid, and the amino acid 827 is asparagine

(see Example XII). The specification teach that the expression pattern of the protein of SEQ ID NO.1 in normal and malignant cells and tissues (see Example XIV).

Guidance in the specification

While one of ordinary skill in the art can theoretically produce all of these protein variants with art known techniques such as site-directed mutagenesis, it would still be burdensome to one of ordinary skill in the art to produce all of these variants and thereafter determine their activity. While the specification teaches that protein of SEQ ID NO.1 is overexpressed in tumor cells, the specification does not teach the tumor expression of the claimed variants. Therefore, one skilled in the art would not know how to use the claimed variants.

Level of skill in the art

The level of the skill in the art is deemed to be high

Conclusion:

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example which teaches how to use the variants of SEQ ID NO.1 and the negative teachings in the prior art balanced only against the high skill level in the art, it

is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 34 and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 200270539A2, Pub. Date: 9/12/2002, effective filing date at least 3/5/2002).

Tang et al. teach a protein of SEQ ID NO.1600 (see claim 9). Because the SEQ ID NO.1600 is 99.8% identical to the instant SEQ ID NO.1, wherein the amino acid 525 is glutamine, and the amino acid 827 is asparagines (see sequence alignment: Exhibit A), the teachings of Tang et al. anticipate claims 34 and 36.

It is noted that the only relevant teachings in Tang et al. reference are the protein of SEQ ID NO.1600 (disclosed in claim 9). Due to the large volume of the cited WO document (total pages 1012), only the relevant pages (pages 1 and 1008) are enclosed in the office action.

Conclusion

11. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
May 15, 2007



LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Exhibit A

<!--StartFragment-->RESULT 4

ABP69553

ID ABP69553 standard; protein; 836 AA.

XX

AC ABP69553;

XX

DT 20-JAN-2003 (first entry)

XX

DE Human polypeptide SEQ ID NO 1600.

XX

KW Human; genome mapping; gene therapy; food supplement; virus; fungus;
 KW cell-proliferative disorder; neurodegenerative disease; bacterial;
 KW Parkinson's disease; Alzheimer's disease; autoimmune disease;
 KW multiple sclerosis; diabetes; genetic disorder; wound; burn; infection;
 KW arthritis; cytostatic; immunomodulator; nootropic; neuroprotective;
 KW antiparkinsonian; antidiabetic; immunosuppressive; dermatological;
 KW haemostatic; vulnerary; fungicide; antibacterial; virucide; protozoacide;
 KW antiarthritic.

XX

OS Homo sapiens.

XX

PN WO200270539-A2.

XX

PD 12-SEP-2002.

XX

PF 05-MAR-2002; 2002WO-US005095.

XX

PR 05-MAR-2001; 2001US-00799451.

XX

PA (HYSE-) HYSEQ INC.

XX

PI Tang YT, Zhou P, Goodrich RW, Asundi V, Zhang J, Zhao QA, Ren F;
 PI Xue AJ, Yang Y, Ma Y, Yamazaki V, Chen R, Wang Z, Ghosh M;
 PI Wehrman T, Wang J, Wang D, Drmanac RT;

XX

DR WPI; 2002-759812/82.

DR

N-PSDB; ABZ11770.

XX

PT New polynucleotides comprising sequences assembled from expressed
 PT sequence tags (ESTs), useful for treating cell-proliferative,
 PT neurodegenerative, autoimmune, genetic, myeloid or lymphoid, or platelet
 PT or coagulation disorders.

XX

PS Claim 9; SEQ ID NO 1600; 1012pp + Sequence Listing; English.

XX

CC The invention relates to an isolated polynucleotide (I) comprising a
 CC nucleotide sequence selected from any of 948 sequences (ABZ11119-
 CC ABZ12066) or their mature protein coding portion, active domain coding
 CC protein or complementary sequences. The polynucleotides are useful for
 CC identifying expressed genes or for physical mapping of human genome. The
 CC encoded polypeptides (ABP68902-ABP69849) are useful as molecular weight
 CC markers, as a food supplement, for generating antibodies, in medical
 CC imaging, screening and diagnostic assays and for treating cell-
 CC proliferative disorders (cancer), neurodegenerative diseases (Parkinson's
 CC or Alzheimer's disease), autoimmune diseases (multiple sclerosis,
 CC diabetes, lupus) genetic disorders, myeloid or lymphoid disorders,
 CC platelet or coagulation disorders, wound, burns, incision, ulcers, liver
 CC or lung fibrosis, infections (bacterial, viral, fungal, parasitic),
 CC arthritis, etc. Note: The sequence data for this patent did not form part
 CC of the printed specification, but was obtained in electronic format
 CC directly from WIPO at ftp.wipo.int/pub/published_pct_sequences

XX

SQ Sequence 836 AA;

Query Match 99.8%; Score 4385; DB 5; Length 836;

Best Local Similarity 99.8%; Pred. No. 0;
Matches 834; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MAGLNCGVSIALLGVLLLGAARLPRGAFAFEIALPRESNITVLIKLGTPDLLAKPCYIVI 60
      |||
Db      1 MAGLNCGVSIALLGVLLLGAARLPRGAFAFEIALPRESNITVLIKLGTPDLLAKPCYIVI 60

Qy     61 SKRHITMLSIKSGERIVFTFSCQSPENHFVIEIQKNIDCMGSPCFGEVQLQPSTSLIPT 120
      |||
Db     61 SKRHITMLSIKSGERIVFTFSCQSPENHFVIEIQKNIDCMGSPCFGEVQLQPSTSLIPT 120

Qy    121 LNRTFIWDVKAHKSIGLELQFSIPRLRQIGPGESCPDGVTHSISGRIDATVVRIGTFCSN 180
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Db    121 LNRTFIWDVKAHKSIGLELQFSIPRLRQIGPGESCPDGVTHSISGRIDATVVRIGTFCSN 180

Qy    181 GTVSRIKMQEGVKMALHLPWFHPRNVSGFSIANRSSIKRLCIIESVFEGEGSATLMSANY 240
      |||
Db    181 GTVSRIKMQEGVKMALHLPWFHPRNVSGFSIANRSSIKRLCIIESVFEGEGSATLMSANY 240

Qy    241 PEGFPEDELMTWQFVVPALHRASVSFLNFNLSNCERKEERVEYIIPGSTTNPEVFKLEDK 300
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Db    241 PEGFPEDELMTWQFVVPALHRASVSFLNFNLSNCERKEERVEYIIPGSTTNPEVFKLEDK 300

Qy    301 QPGNMAGNFNLSLQGCDDQAQSPGILRLQFQVLVQHPQNESNKIYVVDLSNERAMSLTIE 360
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Db    301 QPGNMAGNFNLSLQGCDDQAQSPGILRLQFQVLVQHPQNESNKIYVVDLSNERAMSLTIE 360

Qy    361 PRPVKQSRKFVPGCFVCLESRTCSSNLTLTSGSKHKISFLCDDLTRLWMNVEKTISCTDH 420
      |||
Db    361 PRPVKQSRKFVPGCFVCLESRTCSSNLTLTSGSKHKISFLCDDLTRLWMNVEKTISCTDH 420

Qy    421 RYCQRKSYSLQVPSDILHLPVELHDFSWKLLVPKDRLSLVLVPAQKLQQTKEKPCNTSF 480
      |||
Db    421 RYCQRKSYSLQVPSDILHLPVELHDFSWKLLVPKDRLSLVLVPAQKLQQTKEKPCNTSF 480

Qy    481 SYLVASAIQSDLYFGSFCPGGSIKQIQVKQNISVTLRTFAPSFRQEASRQGLTVSFIPY 540
      |||
Db    481 SYLVASAIQSDLYFGSFCPGGSIKQIQVKQNISVTLRTFAPSFRQEASRQGLTVSFIPY 540

Qy    541 FKEEGVFTVTPDTKSKVYLRTPNWDRGLPSLTSVSWNISVPRDQVACLTFKERSGVVCQ 600
      |||
Db    541 FKEEGVFTVTPDTKSKVYLRTPNWDRGLPSLTSVSWNISVPRDQVACLTFKERSGVVCQ 600

Qy    601 TGRAFMIIQEQRTRAEEIFSLDEDVLPKPSFHHSFWVNISNCSPTSGKQLDLLFSVTLT 660
      |||
Db    601 TGRAFMIIQEQRTRAEEIFSLDEDVLPKPSFHHSFWVNISNCSPTSGKQLDLLFSVTLT 660

Qy    661 PRTVDLTVILIAAVGGGVLLLLSALGLIICCVKKKKKTKNGPAVGIYNGNINTEMPRQPK 720
      |||
Db    661 PRTVDLTVILIAAVGGGVLLLLSALGLIICCVKKKKKTKNGPAVGIYNGNINTEMPRQPK 720

Qy    721 KFQKGRKDNDSHVYAVIEDTMVYGHLLQDSSGSFLQPEVDTYRPFQGTMGVCPSPPTIC 780
      |||
Db    721 KFQKGRKDNDSHVYAVIEDTMVYGHLLQDSSGSFLQPEVDTYRPFQGTMGVCPSPPTIC 780

Qy    781 SRAPTAKLATEEPPPRSPPESESEPYTFSHPNNGDVSSKDTDIPLLSTQEPMEPAE 836
      |||
Db    781 SRAPTAKLATEEPPPRSPPESESEPYTFSHPNNGDVSSKDTDIPLLSTQEPMEPAE 836

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